Improving care in prostate cancer

While outcome has improved in prostate cancer, important deficiencies in care remain. Although chronological age alone should not decide treatment, a man's life expectancy and the presence of serious co-morbid disease are important influences on his choice. In this article, **Mr Greg Boustead** discusses the role of health professionals in helping men to balance the risks and benefits of treatment.

DR GREG BOUSTEAD is a Consultant Urological Surgeon at Lister Hospital, Stevenage

The care of men with prostate cancer is a major challenge for both primary and secondary care. Prostate cancer remains a disease of older men. The ageing of the population together with increasing use of Prostate Specific Antigen (PSA) testing and lower rates of cigarette smoking, probably explains why prostate cancer has overtaken lung cancer as the most commonly diagnosed cancer in men in the UK[1].

Despite a rising incidence, the mortality rates from prostate cancer have declined. There are many possible reasons for this apart from early detection and screening. This includes stage migration, attribution bias, improvements in surgical, radiation and palliative therapy, and earlier and more widespread use of hormonal therapy[2].

Stage migration in prostate cancer has occurred rapidly, and men are now more likely to be diagnosed at a younger age and at an earlier stage when their cancer is potentially curable[3,4]. However, older men are less likely than younger patients to be offered PSA testing and are more likely to present with locally advanced disease[3]. Unfortunately, about 40 per cent of men who originally present with suspected localised disease will show evidence of biochemical failure and progression[5]. As a result, it is crucial to help each patient to make an informed choice of treatment that takes into account his cancer, preferences and circumstances (*Table 1*).

Choice of treatment

Accurate staging and grading of the tumour are essential before making any decision about treatment. Staging of prostate cancer is based on the Tumour Node Metastasis (TNM) classification (*Table 2*), while the tumour is generally graded using the Gleeson score. This system takes into account two factors: the extent to which tumour cells are arranged into glandular structures and the level of cell differentiation. A mixture of cells are present in most prostate tumours, and so the two most prominent grades between one and five are

Table 1. Factors influencing choice of treatment in prostate cancer

Tumour-related factors:
Stage
Grade (Gleeson score)
PSA at diagnosis

Patient-related factors:
Age and general health at diagnosis
Potential impact of treatment on quality of life
Personal preferences.

Table 2. Tumour node metastasis classification of prostate cancer[8]

T: primary tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Clinically inapparent tumour not palpable or visible by imaging
T1a	Tumour incidental histological finding in ≤ 5% of tissue resected
T1b	Tumour incidental histological finding in >5% of tissue resected
T1c	Tumour identified by needle biopsy (for example because of elevated PSA)
T2	Tumour confined within the prostate
T2a	Tumour involves one half of one lobe or less
T2b	Tumour involves more than half of one lobe, but not both lobes
T2c	Tumour involves both lobes
T3	Tumour extends through the prostate capsule
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles or pelvic wall
N: regional lymph nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M: distant metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
MI	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s).

added together to form a prognostic overall score. PSA at diagnosis may also indicate prognosis, which is better if PSA is ≤4ng/ml and worse if it is >20ng/ml.

Although chronological age alone should not decide treatment, a man's life expectancy and the presence of serious co-morbid disease are important influences on his choice. A man also needs to consider not only the potential benefits but also the possible side-effects of each treatment option. Such considerations will have different weight for each patient, since some men are concerned about the side-effects of treatment on their quality of life while others focus on eradicating the tumour. Similarly, men differ in their desire to take an active role in choosing treatment, and each patient's wish should be respected. Doctors are generally poor at estimating patients' life expectancy, and better tools are being developed using actuarial life tables to help physicians and patients in their decision making[6].

The complex interaction of these objective and subjective factors means that it is a challenge in clinical practice to provide patients with definitive advice on treatment, especially in light of the comparative lack of evidence from randomised controlled studies. These difficulties may help to explain (though not excuse) deficiencies in care identified in a recent report from the National Audit Office[7]. Compared with patients with other cancers, men with prostate cancer were more likely to report that they:

- Had not discussed the side-effects and outcome of their treatment
- Would have preferred more information about the outcome of their treatment
- Had not fully understood the explanation of the outcome of their treatment
- Were not given information about support and self-help groups.

The National Audit Office acknowledged that the provision of information has improved in

prostate cancer as in other cancers, and several initiatives have been undertaken as part of the NHS Prostate Cancer Programme to maintain this progress[1]. These include UK Prostate Link, a national prostate cancer website, and action within cancer networks to ensure that men and their families are offered high-quality written information at appropriate points during their care.

In secondary care, specialist nurses within multidisciplinary prostate cancer teams are also playing an increasing role in ensuring that each patient is able to make a truly informed choice about his treatment; but the patient's General Practitioner (GP) is also an essential source of advice and support.

Unlike specialists, GPs are aware of the man's family background and social circumstances, and some men may prefer to discuss their options with their trusted GP at the local surgery rather than with an unfamiliar professional in a busy hospital clinic.

Current approaches to treatment

Localised prostate cancer

The aim of treatment in localised prostate cancer (stages T1–T2) is either to eliminate the tumour or to minimise disease progression during the lifetime of the patient. Both these objectives can be achieved by the current standard therapies of surgery with radical prostatectomy, radiotherapy, or deferred treatment.

Overall 10-year survival rates following radical prostatectomy range from 47 to 75 per cent[8], and this option is generally recommended for younger men (life expectancy >10 years). Patients should be informed that, since radical prostatectomy involves removal of the entire prostate gland, seminal vesicles and adjacent tissue, there is a risk of long-term complications including stress incontinence (five per cent) and Erectile Dysfunction (ED) in 40 to 70 per cent. Men should also be aware of the risks, albeit low, of perioperative death and major bleeding requiring blood transfusion.

Radiotherapy is the primary mode of treatment for men who choose active treatment but are unable or unwilling to undergo radical prostatectomy, and it may also be combined with surgery in men with a high risk of recurrent disease. ED is less likely with radiotherapy

than with radical prostatectomy, but urinary incontinence and chronic diarrhoea remain important concerns.

Some patients may prefer less invasive procedures such as cryotherapy and High-Intensity Focused Ultrasound (HIFU), which were both recently appraised by the *National Institute for Health and Clinical Excellence (*NICE)[9,10]. On currently available evidence, these procedures appear to be effective in reducing PSA, but longer follow-up is needed to confirm that these treatments are as effective as standard therapies in reducing the risk of recurrence and improving survival.

Since prostate cancer is a slow-growing tumour, surveillance with regular PSA checks and if necessary deferred treatment remains a reasonable option for older patients (life expectancy <10 years) with well or moderately differentiated tumours, especially if they have other significant co-morbidities and wish to avoid invasive treatment. Some men may, however, find it psychologically difficult to cope with the presence of the untreated tumour.

Locally advanced prostate cancer

In men with locally advanced disease (stage T3), the aim of the treatment is to prolong survival by reducing the risk of metastases. Watchful waiting remains a valid option for men with minimal symptoms and/or a short life expectancy and co-morbid disease, since they are likely to experience reduced quality of life from the adverse effects of treatment without compensatory benefit in terms of survival. However, such men must receive regular follow-up and palliative treatment as necessary to relieve symptoms such as urinary complications.

The mainstay of active treatment is a combination of radiotherapy and androgen deprivation, especially in aggressive, high-volume, locally advanced disease. Both neoadjuvant and adjuvant hormonal treatment with a Luteinising Hormone Releasing Hormone (LHRH) analogue has improved survival in randomised studies[11-14]. The timing and duration of hormonal therapy remains unclear and, because of the risk of side-effects, the aim in clinical practice is to administer treatment for as short a time as possible without compromising patient survival. Most experts agree that in high-risk prostate cancer (Gleeson 8,9,10; Node +ve; stage T3/4), adjuvant hormone therapy should continue for a minimum of two to three years.

UK Prostate Link

The UK Prostate Link website (www.prostate-link.org.uk) is aimed at men with prostate cancer, their family caregivers, and healthcare professionals, and is supported by a range of organisations concerned with prostate cancer. The aim of the site is to act as a first port of call for prostate cancer information by providing a searchable database of links to prostate cancer information on the internet. UK Prostate Cancer Link directly assesses the quality of the information so that users can be directed to the best prostate cancer resources on the web.

Long-term follow-up of the Early Prostate Cancer (EPC) study[15] has recently shown that radiotherapy and adjuvant treatment with the non-steroidal anti-androgen bicalutamide also improves survival compared to radiotherapy alone. In addition, the risk of bone metastases was significantly reduced with bicalutamide both when used as adjuvant therapy or as monotherapy. The EPC study has important implications for clinical practice, since men now have an alternative treatment with a side-effect profile that differs from that of LHRH analogues. In particular, although bicalutamide is more likely to be associated with hot flushes and breast tenderness, there is less risk of the ED, fracture and fatigue that are seen with LHRH analogues.

Metastatic prostate cancer

Androgen deprivation with an LHRH analogue, non-steroidal anti-androgen or orchidectomy remains first-line treatment in men with advanced prostate cancer (stage T any, M+ve), when the aim is to maintain quality of life by preventing or controlling symptoms of disease progression or complications. Maximal Androgen Blockade (MAB) with the combination of a non-steroidal anti-androgen and a LHRH analogue improves survival after five years follow-up, but is associated with an increased risk of side-effects[16].

Most prostate cancers eventually become refractory to androgen deprivation treatment.

Key points

- Prostate cancer is now the most commonly diagnosed cancer among men in the UK.
- More men are being diagnosed with early-stage disease, where there are several alternative treatments.
- Treatment for men with advanced prostate cancer is improving following results of recent randomised controlled studies.
- All treatments for prostate cancer are associated with side-effects that some men may find unacceptable.
- It remains a challenge for health professionals to ensure that each patient is able to make an informed choice for treatment that is appropriate for the stage and grade of his cancer, and his personal circumstances and preferences.

Second- and third-line hormonal interventions, such as addition or withdrawal of anti-androgens and diethylstilbestrol often show PSA responses, but no hard evidence exists that this improves survival. Other supportive measures include bisphosphonates or short courses of palliative radiotherapy to reduce bone complications, corticosteroids, and palliative treatment to relieve pain.

Until recently, conventional systemic chemotherapy showed poor response rates in prostate cancer. For the first time, however, two recent randomised studies[17,18] showed modest but significant improvements in survival with docetaxel. However, men need to weigh this benefit against the risk of adverse effects such as anaemia, neutropenia, infection, nausea and fatigue.

Furthermore, while docetaxel in combination with prednisolone is licensed in the UK for hormone-resistant prostate cancer, the Scottish Medicines Consortium recently decided not to recommend docetaxel on the basis of lack of cost-effectiveness and NICE appraisal is not scheduled for publication until summer 2006.

Conclusion

The establishment of multidisciplinary prostate cancer teams in secondary care has undoubtedly improved the care of men with prostate cancer.

This process looks set to continue as the results of recent randomised studies are translated into clinical practice, and more patients will hopefully be given the opportunity to enter important clinical trials.

Improved provision of information and the possible introduction of validated decision-making tools[1] should help to improve patient awareness, but it will remain the responsibility of healthcare professionals to ensure that all patients are able to make a truly informed choice about their treatment ■ GM

Conflict of interest: Mr Boutstead has acted as consultant advisor, speaker or investigator for the following companies: Astellas, AstraZeneca, Eli Lilly, Gynecare, GPC Biotech and GlaxoSmithKline

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